Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The pathogenesis of potential myocarditis induced by COVID-19 vaccine

Myocarditis is often attributed to a viral infection, however other forms such as hypersensitivity, autoimmune and idiopathic, have contributed to the disease induction. Rare cases of COVID-19 vaccine induced-myocarditis, especially in young men have been reported [1]. In a recent report, 21 persons presented with myocarditis post Pfizer-BioNTech (BNT 162b2) mRNA Covid-19 Vaccine administration, with a median age of 25 years (interquartile range, 20 to 34), and 90.9% male predominance [2]. Interestingly, most of the cases were reported after the second dose with a median onset of symptoms, approximately, three days post vaccination. In the Vaccine Adverse Event Reporting System (VAERS) nearly 1300 cases were demonstrated out of more than 350 million doses in the United States [3]. However, these cases were characterized according to Centers for Disease Control and Prevention (CDC) as probable myocarditis, confirmed myocarditis, or acute pericarditis [4]. Myocarditis after COVID-19 vaccination initially was reported with mRNA vaccines but, recently, the United Kingdom Medical and Health Care products Regulatory Agency (MHRA) adverse event report revealed 31 cases of myocarditis related with AstraZeneca vaccine as well [5].

In the very interesting report published in the American Journal of Emergency Medicine [6], a 20-year-old healthy male developed myocarditis with small pericardial effusion 2 days post the second dose administration of the BNT 162b2 vaccination. The patient underwent left heart catheterization that was unremarkable but myocardial biopsy was not performed, presumably, due to the patient's low-risk profile and favorable progress. The authors concluded that a true cause-and-effect relationship could not be established nor determined. Indeed, the pathogenesis of COVID-19 vaccine-associated myocarditis is poorly understood due to its mild clinical course and the lack of myocardial biopsy performance. However, histological or immunohistological evidence of an inflammatory cell infiltration with or without corresponding myocardial damage is the gold standard for myocarditis diagnosis. Hypersensitivity, eosinophilic, and lymphocytic myocarditis are distinct conditions with a debate concerning their pathophysiology. Hypersensitivity or drug induced myocarditis occurs after hypersensitivity reactions to drugs or substances and is neither necrotizing nor fibrotic [7,8]. Peripheral eosinophilia might be absent that renders clinical diagnosis difficult [9]. Drugs and substances that can cause hypersensitivity myocarditis include vaccines, antibiotics, central nervous system drugs, antitubercular agents and a variety of other undetermined drugs [10]. Hypersensitivity myocarditis can occur in 3% to 10% of cardiac explants and in patients with a ventricular assist device. One third of patients may demonstrate no peripheral eosinophilia and most patients respond well to steroids and drug cessation [9]. Two such cases have been recently diagnosed 2 weeks post BNT162b2 COVID-19 vaccination with endomyocardial biopsies revealing eosinophils and other interacting inflammatory cells such as macrophages, T-cells, and B cells [11]. Eosinophilic myocarditis is a necrotizing disease resembling to hypereosinophilic syndromes (Loeffler endomyocarditis) and eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) [9]. Lymphocytic myocarditis with presence of macrophages and T cells has been diagnosed after BNT162b2 COVID-19 vaccination, but staining with hematoxylin-eosin to identify eosinophils was not performed [12]. All COVID-19 vaccines contain, as emulsifiers, polysorbate (AstraZeneca, Johnson &Johnson) or polyethylenglycol (BNT162b2, Moderna) that are also present in creams, ointments, lotions, other cosmetics, anti-cancer drugs and various dental materials. Rarely, these can act as antigens and can further sensitize their users. Indeed, 1–5.4% of the population is already sensitized to cosmetics or dental materials [13]. Therefore, hypersensitivity or drug-induced myocarditis could be the result of hypersensitivity to the above materials. Alternatives in vaccine manufacturing have been already suggested if vaccine component-induced hypersensitivity is confirmed but more systematic future investigations are needed [14]. Indeed, free polysorbate oncology medications are already available in the market [15]. Alkylsaccharides constitute promising agents as they can reduce immunogenicity, improve stability, suppress oxidative damage and prevent thrombotic and cardiovascular events [16]. Undoubtedly, COVID-19 free allergenic vaccines might prove more appropriate and beneficial without inducing such, rare, cardiovascular events.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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